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containing an engineered C terminal cysteine (Tox): VL, L, VH, H,  $\gamma$ CH3,  
His6, Cys-SH-R-SH-Tox.--

REMARKS

The Examiner objected in his communication dated June 17, 2002, stating that "the Cys-S-R-S sequence of page 16 of the specification must be brought into sequence compliance."

Applicants respectfully traverse on the ground that the entire application is in compliance with the requirements related to nucleotide and amino acid sequences.

The text of the specification describes one embodiment of the invention as an "sFv-SH fusion protein homodimerized via H 226/229 Cys chemically linked via a bis maleimide (R) to a SH derivatized CRM9 or a CRM9 containing an engineered C terminal cysteine (Tox)" and then gave as further explanation the following order for the components of the fusion protein: "VL, L, VH, H,  $\gamma$ CH3, His6, Cys-S-R-S-Tox." The description taken as a whole makes clear that the Applicants were not intending to mix three-letter and one-letter amino acid abbreviations in their use of the term "Cys-S-R-S." The text makes clear that the construct includes a cysteine residue linked via a sulfhydryl group to a bis maleimide, which is linked to a toxin residue via another sulfhydryl group. Thus, each "S" in the reference "Cys-S-R-S" refers, not to a serine residue, but to a sulfhydryl group. Under 37 C.F.R. § 1.821, sequences of less than four amino acids are specifically excluded from the formalities required for longer sequences. Cysteine linked to a bis

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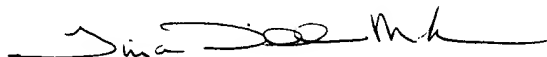
malemide does not constitute four or more amino acids and the term "Cys-S-R-S" without further designation of SEQ ID NO is in complete compliance with the rules.

Applicants, nonetheless, in an effort to facilitate prosecution of this application, amend the specification herein to clarify that the term "Cys-S-R-S-Tox" does not refer to a four amino acid sequence. Specifically, the reference is amended to use "SH" rather than "S" to refer to the sulfhydryl groups as follows: "Cys-SH-R-SH-Tox." Support for the amendment can be found on page 16, line 6 which refers to a SH derivatized CRM9.

Applicants assert that this amendment adds no new matter and respectfully request entry of this amendment. A marked-up copy of the amended paragraph is attached as Appendix A.

No fee is believed due. However, the Commissioner is hereby authorized to charge any additional fees that may be required to Deposit Account No. 14-0629.

Respectfully submitted,


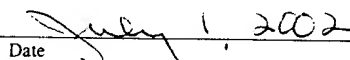


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CERTIFICATE OF AMILING

I hereby certify that this correspondence and anything indicated as attached or enclosed is being deposited with the United States Postal Service as first class mail in an envelope addressed to: BOX NON-FEE AMENDMENT, Commissioner of Patents, Washington, D.C. 20231, on the date shown below.

  
Tina Williams McKeon  
Date

**Appendix A**  
**Marked-Up Version of Amended Paragraphs**

Paragraph on page 15, line 19, through page 16, line 8:

--Single chain divalent fusion protein: Tox, VL, L, VH, L, VL, L, VH;

Single chain univalent fusion protein homodimerized via  $\mu$ CH2 337 Cys: (Tox, VL, L, VH,  $\mu$ CH2)2;

Single chain univalent fusion protein homodimerized via H 226/229 Cys: (Tox, VL, L, VH, H,  $\gamma$ CH3)2;

Single chain univalent fusion protein heterodimerized via  $\mu$ CH2 337 Cys: (Tox, VL, L, VH,  $\mu$ CH2  
VL, L, VH,  $\mu$ CH2);

Single chain univalent fusion protein heterodimerized via H 226/229 Cys: (Tox, VL, L, VH, H,  $\gamma$ CH3  
VL, L, VH, H,  $\gamma$ CH3);

sFv-SH fusion protein homodimerized via H 226/229 Cys chemically linked via a  
bis maleimide (R) to a SH derivatized CRM9 or a CRM9 containing an  
engineered C terminal cysteine (Tox): VL, L, VH, H,  $\gamma$ CH3, His6, Cys-SH-R-SH-  
Tox.--